38. (Amended) The potassium channel of Claim 36 wherein direction and magnitude of potassium current is modulated by external potassium in concentration.

39. (Amended) The potassium channel of Claim 36 wherein potassium is the permeant ion.

REMARKS

By this Amendment, the specification and claims 4-13, 16, 19, 24-26, 29-32, 38, and 39 are amended. The specification is amended to recite Sequence Identifiers consistent with the Sequence Listing. The claims are also amended to recite Sequence Identifiers consistent with the Sequence Listing and to correct improper dependencies. Accordingly, no new matter is added by this Amendment. Currently, claims 1-33 and 36-39 are pending in this application.

I. *Restriction Requirement*

In a second Restriction Requirement, dated December 31, 2001, the Office withdraws the original Restriction Requirement and asserts a new one. In the second Restriction Requirement, the Office restricts the claims into twelve (12) Groups, and requires Applicants to elect one of the Groups for examination in this application. In response to the Restriction Requirement, Applicants provisionally elect Group VI, claims 22, 24, 27, 29, 30, and 33, *with* traverse.

It is respectfully submitted that the subject matter of all of claims 1-33 and 36-39 are sufficiently related that a thorough search of the subject matter of any one Group of claims would encompass a search for the subject matter of the remaining claims. Thus, a search and

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
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examination of the non-elected claims with the claims of Group VI would not place a serious additional burden on the Examiner. MPEP § 803 states that "if the search and examination of the entire application can be made without serious burden, the examiner must examine it on the merits" (emphasis added herein by Applicants). It is respectfully submitted that this policy should apply in the present application in order to avoid unnecessary delay and expense to Applicants and duplicative examination by the Patent Office.

Furthermore, Applicants respectfully submit that the Office has improperly limited the scope of the claims through the Restriction Requirement. For example, in issuing the Restriction Requirement, the Office has, without Applicants' permission or approval, limited the scope of claims 1 and 22 to the specific species claimed in dependent claims. Applicants respectfully submit that they have a statutory right under 35 U.S.C. § 112, second paragraph, to claim the subject matter they regard as their invention as they choose. Issuing a Restriction Requirement by incorporating an unclaimed limitation in an effort to limit the claim to disclosed embodiments, with the idea that Applicants would have to carve up that claim and pursue the non-elected subject matter in a separate application, violates this right under § 112. Indeed, the C.C.P.A. has characterized such action as tantamount to a refusal to examine. *See In re Weber*, 198 U.S.P.Q. 328 (C.C.P.A. 1978); *In re Haas*, 198 U.S.P.Q. 334 (C.C.P.A. 1978).

In addition, the Restriction Requirement makes it impossible for Applicants to obtain the full scope of their invention, even if every Group were to be pursued in all twelve applications that would be required as a result of the Restriction Requirement. That is, even if Applicants pursued each and every Group set forth in the Restriction Requirement, they still would not obtain full coverage for claim 1, which generically recites a potassium channel comprising four

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hydrophobic domains capable of forming transmembrane helices and two pore-forming domains interposed between the first and second and the third and fourth transmembrane helices. Thus, the Restriction Requirement is improper because it completely eliminates subject matter from the application.

In addition to the outright elimination of claimed subject matter from claim 1, subject matter from claim 22 has been eliminated from this application through the Restriction Requirement as well. Specifically, the true scope of claim 22 includes all isolated nucleotide sequences capable of encoding a protein designated CORK. Claim 22 is not limited in scope to SEQ ID NO:36. Thus, the subject matter encompassed by claim 22, but not covered by SEQ ID NO:36, has been completely eliminated from the application by the Restriction Requirement. Such an action is improper and impermissible.

In the event that the Office does not withdraw the Restriction Requirement, Applicants respectfully submit that the non-elected method claims of Group XII should be rejoined with the product claims of Group VI, once one or more product claims are found to be allowable. In response to *In re Ochiai* and *In re Brouwer,* the Commissioner set forth guidelines for treatment of non-elected process claims. *See* the Official Gazette, 1184 OG 88 (March 26, 1996). These guidelines have been incorporated into MPEP § 821.04. Under these PTO guidelines, "rejoinder practice" applies to Applicants who have elected claims to a product over claims to a process in compliance with a Restriction Requirement. When it is established that a product claim is allowable, withdrawn process claims that depend from, or otherwise include all the limitations of, the allowable product claim must be rejoined. Applicants respectfully submit that this procedure applies to the present claims of Groups VI and XII.

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1300 I Street, NW
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In view of the above remarks, Applicants request reconsideration and withdrawal of the Restriction Requirement. Furthermore, Applicants request re-joinder of Group XII with elected Group VI. In the event that the Office does not withdraw the Restriction Requirement, Applicants reserve the right to appeal the Restriction Requirement and/or to prosecute the non-elected claims in divisional or continuation applications.

II. *Sequence Rules*

The Restriction Requirement further asserts that the application does not comply with the Sequence Rules. (Restriction Requirement at paragraph 3, page 4.) Applicants' undersigned representative contacted the Examiner by telephone on January 7, 2002, to determine why the application did not comply. During the telephone conference, the Examiner agreed that the application does comply with the Sequence Rules, but that the Brief Description of Figure 3 was incomplete. The Examiner also indicated that it would be helpful for examination of this application if Applicants submitted a concise listing of the Sequence Identifiers and the sequences to which they correspond.

In response, Applicants hereby amend the specification at page 8 to properly recite the Sequence Identifiers presented in Figure 3. Applicants have also amended the specification at pages 59-60 to properly recite Sequence Identifiers in accordance with the Sequence Listing. Furthermore, attached hereto is a listing of the Sequence Identifiers disclosed in the application and a brief identification of the corresponding nucleic acid or protein sequences.

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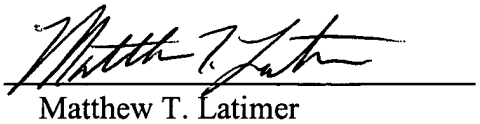
III. *Conclusion*

Applicants respectfully request reconsideration and withdrawal of the Restriction Requirement, and early and favorable examination of this application. If the Examiner believes anything further is necessary in order to place this application in better condition for allowance, he is invited to contact Applicants' undersigned representative at the telephone number or e-mail address listed below.

Please grant any extensions of time required to enter this response and charge any required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

By: 

Matthew T. Latimer
Reg. No. 44,024
(202) 408-4495
matthew.latimer@finnegan.com

Date: January 28, 2002

Attachments:
Appendix
List of Sequence Identifiers

FINNEGAN
HENDERSON
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DUNNER LLP

1300 I Street, NW
Washington, DC 20005
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APPENDIX

08/816,011

IN THE SPECIFICATION:

Please replace the second paragraph on page 8 with the following new paragraph:

-- FIGURE 3A and 3B. DNA sequence and deduced amino acid sequence of the F22b7.7 segment of the *Caenorhabditis elegans* genome, ([[]SEQ ID NO:3[]] and SEQ ID NO:4), respectively. Segments corresponding to putative transmembrane (M1-M4) and pore-forming H5 domains in the predicted polypeptide are underlined.--

Please replace the paragraph bridging page 59, line 2 to page 60, line 2, with the following new paragraph:

-- In order to expand the applicability of this technology to discover compounds with novel anhelmenthic activity, CY162 cells were transformed with a pYES2-based yeast expression library constructed using cDNA synthesized from *C. elegans* mRNA (Invitrogen). Plasmid DNA isolated from yeast cells that survived the selection scheme described in EXAMPLE 1 were subjected to automated DNA sequence analysis performed by high temperature cycle sequencing (Applied Biosystems). Geneworks DNA sequence analysis software (Intelligenetics) is used to align raw DNA sequence information and to identify open reading frames. The DNA sequence of the 1.4 kb insert in pCORK, and the encoded protein, [is] are displayed in FIGURE 9A and 9B ([[]SEQ ID NO: 36 and SEQ ID NO:63, respectively)[]]. The 5' untranslated sequences of the cDNA are present in this construct. A single long open reading frame sufficient to encode a

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protein of 434 amino acids (predicted MW 48 kDa) is predicted in pCORK. A consensus polyadenylation site, AATAAA, occurs at position 1359-1364 in 3' untranslated sequences and is followed by a tract of 15 consecutive A residues. The CORK ORF contains structural features that resemble pore forming H5 domains found in potassium channels. Two putative pore forming H5 domains (residues 76-39 and 150-162) contain the G-Y/F-G tripeptide motif required for potassium selectivity [[](Heginbotham *et al.*, Science 258, 1152-1155, (1992))[[].--

IN THE CLAIMS:

Please amend claims 4-13, 16, 19, 24-26, 29-32, 38, and 39 as follows:

4. (Amended) The potassium channel of Claim 3 wherein the pore-forming domain comprises [ZXXZ$_1$Z$_2$Z$_4$GXG] SEQ ID NO:57, wherein

(i) [Z through Z$_2$] X at positions 1, 4, and 5 are [amino acid residues comprising] T or S;

(ii) [Z$_3$] X at position 6 is [an amino acid residue comprising] I or V; and

(iii) X at position 8 is [an amino acid residue comprising] V, L, Y, F, M, or I.

5. (Amended) The potassium channel of Claim 4 where X at position 8 is L or I.

6. (Amended) The potassium channel of [Claims] Claim 1, [2, 3, 4, or 5] wherein at least one pore-forming domain is positioned proximal to an exterior portion of a cell membrane.

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7. (Amended) The potassium channel of Claim 5 further comprising [an amino acid motif $ZX_1X_2X_3GX_4PX_5$] SEQ ID NO:58 downstream of said first pore-forming domain.

8. (Amended) The potassium channel of Claim 7 wherein[$ZX_1X_2X_3GX_4PX_5$] SEQ ID NO:58 is positioned about 12-25 amino acids downstream of said first pore-forming domain.

9. (Amended) The potassium channel of Claim 8 wherein [$ZX_1X_2X_3GX_4PX_5$] SEQ ID NO:58 is positioned within the second transmembrane domain.

10. (Amended) The potassium channel of Claim 8 [or 9] wherein [$ZX_1X_2X_3GX_4PX_5$] SEQ ID NO:58 is positioned beginning about 16 amino acids downstream of said first pore-forming domain.

11. (Amended) The potassium channel of Claim 8, [9 or 10] wherein a second [$ZX_1X_2X_3GX_4PX_5$] peptide comprising SEQ ID NO:58 is located within said second pore-forming region.

12. (Amended) The potassium channel of Claim 8, [9, or 10] wherein [$ZX_1X_2X_3$ comprises] X at positions 1-4 are the amino acids YALL.

13. (Amended) The potassium [channels] channel of Claim 12 wherein [$ZX_1X_2X_3GX_4P$ comprises] SEQ ID NO:58 is the amino acids YALLGIP.

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16. (Amended) The potassium channel of [Claims] Claim 1, [2, 3, 4, 5, 7, or 8] characterized in that it is derived from invertebrates.

19. (Amended) The potassium channel of [Claims] Claim 1, [2, 3, 4, 5, 6, 7, or 8] characterized in that it is derived from vertebrates.

24. (Amended) An isolated nucleotide sequence comprising

(i) [a] the nucleotide sequence [depicted in] of SEQ ID NO:1 or SEQ ID NO:36;

(ii) a nucleotide sequence that hybridizes to said sequence [depicted in] of SEQ ID NO:1 or SEQ ID NO:36;

(iii) a nucleotide sequence that is degenerate to the nucleotide sequence [depicted in] of SEQ ID NO:1 or SEQ ID NO:36; [and] or

(iv) a functional derivative of the nucleotide sequence [depicted in] of SEQ ID NO:1 or SEQ ID NO:36.

25. (Amended) An isolated nucleotide sequence comprising

(i) [a] the nucleotide sequence [depicted in] of SEQ ID NO:46;

(ii) a nucleotide sequence that hybridizes to said sequence [depicted in] of SEQ ID NO:46;

(iii) a nucleotide sequence that is degenerate to the nucleotide sequence [depicted in] of SEQ ID NO:46; [and] or

(iv) a functional derivative of the nucleotide sequence [depicted in] of SEQ ID NO:46.

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26. (Amended) An isolated nucleotide sequence comprising

(i) [a] the nucleotide sequence [depicted in] of SEQ ID NO:51, SEQ ID NO:52, or SEQ ID NO:53;

(ii) a nucleotide sequence that hybridizes to said sequence [depicted in] of SEQ ID NO:51, SEQ ID NO:52, or SEQ ID NO:53;

(iii) a nucleotide sequence that is degenerate to the nucleotide sequence [depicted in] of SEQ ID NO:51, SEQ ID NO:52, or SEQ ID NO:53; [and] or

(iv) a functional derivative of the nucleotide sequence [depicted in] of SEQ ID NO:52, SEQ ID NO:52, or SEQ ID NO:53.

29. (Amended) An expression vector capable of expressing the potassium channel encoded by the nucleotide sequence of [Claims] Claim 24[, 25, or 26] in a cell membrane of a yeast cell.

30. (Amended) A transformed yeast cell comprising the expression vector of [Claims] Claim 27[, 28, or 29].

31. (Amended) A method of assaying substances to determine effects on cell growth, the method comprising the steps of:

a) preparing cultures of yeast cells in a medium adequate to support growth of potassium-dependent mutant strains expressing the [potassium channel of Claim 1] nucleotide sequence of Claim 22;

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b) contacting said substance to a portion of said yeast cells thereafter permitting sufficient time for continued growth, if any, of the portion of yeast cells so contacted as well as the portion not contacted with said substance;

c) identifying zones of growth around the substances, wherein the level of growth indicates whether or not activity of the heterologous potassium channel has been modulated as compared to yeast cells not contacted with said substances.

32. (Amended) The method of Claim 31 wherein said yeast cells comprise the nucleotide sequence of [Claims 24, 25, or 26] SEQ ID NO:1, SEQ ID NO:36, SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, or SEQ ID NO:53.

38. (Amended) The potassium channel of Claim 36 [or 37] wherein direction and magnitude of potassium current is modulated by external potassium in concentration.

39. (Amended) The potassium channel of Claim 36 [or 37] wherein potassium is the permeant ion.

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List of Sequence Identifiers
(attachment to Response of January XX, 2002)

08/816,011

Sequence Identifier	Description of Corresponding Sequence
1	DNA sequence of Dm ORF1
2	Deduced amino acid sequence of Dm ORF1
3	DNA sequence of the F22b7.7 segment of the *C. elegans* genome
4	Deduced amino acid sequence encoded by the F22b7.7 segment of the *C. elegans* genome
5	Oligonucleotide for amplification of pore-forming domains of F22b7.7
6	Oligonucleotide for amplification of pore-forming domains of F22b7.7
7	Pore-forming domain from the mouse inward rectifier potassium channel Kir2.1
8	Pore-forming domain from the human rod outer medullary (kidney) inward rectifier potassium channel Kir1.1a
9	Pore-forming domain from rat G protein coupled inward rectifier potassium channel Kir3.1
10	First pore-forming region from the *D. melanogaster* channel
11	*D. melanogaster* shaker pore-forming region
12	*D. melanogaster* sha1 pore-forming region
13	*D. melanogaster* Shab pore-forming region
14	*D. melanogaster* Shaw pore-forming region
15	*D. melanogaster* Eag pore-forming region
16	*D. melanogaster* Slo pore-forming region

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17	Second pore-forming region from the *D. melanogaster* channel
18	First pore-forming region from the *D. melanogaster* channel
19	First pore-forming region from the *C. elegans* channel
20	Second pore-forming region from the *D. melanogaster* channel
21	Second pore-forming region from the *C. elegans* channel
22	Oligonucleotide for amplification of DmORF1 coding region
23	Oligonucleotide for amplification of DmORF1 coding region
24	Oligonucleotide for amplification of *D. melanogaster* shaker gene
25	Oligonucleotide for amplification of *D. melanogaster* shaker gene
26	Oligonucleotide for amplification of *D. melanogaster* shab gene
27	Oligonucleotide for amplification of *D. melanogaster* shab gene
28	Oligonucleotide for amplification of *D. melanogaster* sha1 gene
29	Oligonucleotide for amplification of *D. melanogaster* sha1 gene
30	Oligonucleotide for amplification of *D. melanogaster* shaw gene
31	Oligonucleotide for amplification of *D. melanogaster* shaw gene
32	Oligonucleotide for amplification of *D. melanogaster* Eag gene
33	Oligonucleotide for amplification of *D. melanogaster* Eag gene
34	Oligonucleotide for amplification of *D. melanogaster* Slo gene
35	Oligonucleotide for amplification of *D. melanogaster* Slo gene
36	Nucleotide sequence of CORK
37	Fragment of Dm ORF1
38	Fragment of F22b7.7

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39	Degenerate oligonucleotide primer for amplification of human two-pore potassium channels according to the invention
40	Degenerate oligonucleotide primer for amplification of human two-pore potassium channels according to the invention
41	Oligonucleotide primer for RACE cloning of human two-pore potassium channels according to the invention
42	Oligonucleotide primer for RACE cloning of human two-pore potassium channels according to the invention
43	Oligonucleotide primer for completion of cloning of hORK1
44	Oligonucleotide primer for completion of cloning of hORK1
45	Deduced amino acid sequence of hORK1 protein
46	Nucleotide sequence of hORK1 gene
47	Oligonucleotide primer for subcloning hORK1 ORF into pLP100
48	Oligonucleotide primer for subcloning hORK1 ORF into pLP100
49	Oligonucleotide primer for subcloning hORK1 ORF into pYES2
50	Oligonucleotide primer for subcloning hORK1 ORF into pYES2
51	Open reading frame of cDNA (human) clone 277113, encoding a portion of a channel according to the invention
52	Open reading frame encoding a murine channel according to the invention (combined sequence from clones 303895, 421453, and 334194)
53	Open reading frame of murine cDNA clone 333546, encoding a portion of a channel according to the invention
54	Deduced amino acid sequence of the protein fragment encoded by human cDNA clone 277113 (identical to SEQ ID NO:61)
55	Deduced amino acid sequence of the open reading frame of SEQ ID NO:52, encoding a portion of a channel according to the present invention (this sequence is identical to SEQ ID NO:62)

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56	Deduced amino acid sequence of the protein fragment encoded by the open reading frame of SEQ ID NO:53 (murine)
57	Peptide motif in one or both pore-forming regions of channels according to the invention
58	Peptide motif in one or both pore-forming regions of channels according to the invention
59	One embodiment of peptide motif in the first pore-forming region of channels according to the invention
60	One embodiment of peptide motif in the first pore-forming region of channels according to the invention
61	Deduced amino acid sequence of the protein fragment encoded by human cDNA clone 277113 (this sequence is identical to SEQ ID NO:54)
62	Deduced amino acid sequence of the open reading frame of SEQ ID NO:52, encoding a portion of a channel according to the present invention (this sequence is identical to SEQ ID NO:55)
63	Deduced amino acid sequence of CORK
64	Consensus sequence of at least 4 contiguous amino acids between DmORF1 and CeORF1
65	Consensus sequence of at least 4 contiguous amino acids between DmORF1 and CeORF1
66	Consensus sequence of at least 4 contiguous amino acids between DmORF1 and CeORF1
67	Consensus sequence of at least 4 contiguous amino acids between DmORF1 and CeORF1

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